UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/696,867	10/25/2000	Mary E. Brunkow	240083.501D6	2612

500 7590 06/05/2002

SEED INTELLECTUAL PROPERTY LAW GROUP PLLC
701 FIFTH AVE
SUITE 6300
SEATTLE, WA 98104-7092

EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	7

DATE MAILED: 06/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/696,867	BRUNKOW ET AL.	
	Examiner	Art Unit	
	S. Kaushal	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice toComply* .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group VI (claim 34) in Paper No. 6 is acknowledged.

Claims 12-23 and 26-33 are canceled.
Claim 34 is pending and is examined in this office action.

► *If the claims are amended, added and/or canceled in response to this office action the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (http://www.uspto.gov) and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED.*

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 34 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic scurfy mouse whose cells express a transgene that contain a sequence encoding mouse Fkh^{sf} protein wherein the expression of exogenous Fkh^{sf} transgene results in reduction of lymphocyte proliferation in the mouse, does not reasonably provide

enablement for any and all transgenic non-human animals whose cells express a transgene the contain a Fkh^{sf} coding sequence obtained from any and animals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches that mice hemizygous for the scurfy mutation exhibit a severe lymphoproliferative disorder (spec. page 1-2). The specification teaches the identification of and cloning of gene responsible for the scurfy phenotype in mouse. (spec. page 32, example-1.A). The specification further teaches microinjection of Fkh^{sf} DNA into normal one-cell mouse embryos and disclosed the production of five founder mice (spec. page 33, example-1.b). The specification discloses the mating of male Fkh^{sf} transgenic animals with female *sf* carriers and characterization of male offspring carrying both Fkh^{sf} transgene and *sf* mutation (spec. page 33, line 10-17). The specification further disclosed that analysis of *sf* progeny reviled that the expression of Fkh^{sf} transgene in *sf* mice over come the lymphoproliferative defect found in scurfy mice (spec. page 33, line 25-27, figures 6-8).

The invention as claimed is drawn to a non-human transgenic animal whose cells express a transgene that contain a sequence encoding Fkh^{sf} protein. The scope of instant invention as claimed encompasses any and all non-human transgenic animals (insects, fish, reptiles, birds and mammals like whale, pigs, cow and elephant). At best the specification only discloses a transgenic scurfy mouse whose cells express a transgene that contain a sequence encoding mouse Fkh^{sf} protein, wherein the expression of exogenous Fkh^{sf} transgene results in reduction of lymphocyte proliferation in the mouse. The specification fails to disclose any other animal whose cells express a transgene that contain a sequence encoding Fkh^{sf} protein, wherein the sequence encoding Fkh^{sf} transgene has been obtained from any and all organisms. The state of transgenic art at the time of filing was such that phenotype of an animal is determined by a complex interaction of genetics and environment. (Wood. Comp. Med. 50(1): 12-15, 2000, see page12). The phenotype examined in a transgenic and knock out model is influenced by genetic background, which is the collection of all genes present in an organism that influence a trait or traits. The genes may be part of same biochemical or signaling pathway or of an opposing pathway or may appear unrelated to the gene being studied. Furthermore, allelic variations and the interactions between the allelic variants also influence a particular phenotype. These

epigenetic effects can dramatically alter the observed phenotype and therefore can influence or alter the conclusions drawn form the transgenic or knockout models (Sigmund, Arterioscler. Throm. Vasc. Biol.20:1425-1429, 2000, see page 1425).

The transgene expression and physiological consequences of transgene products in non-mouse mammals are not always accurately predicted among various species of mammals (Wall RJ Theriogenology 45:57-68, 1996). Transgene efficiency is low, and range from 1% in farm animals (cattle, sheep, pigs) to 3% in laboratory animals like rabbits, mice and rats (Wall, see page 61). Furthermore, the lack of understanding of essential genetic control elements make it difficult to predict the behavior of a transgene in any and all animals because the expression is influenced by position effect in transgenic animals. The individual gene of interest, promoter, enhancer, coding or non-coding sequences present in the transgene construct and the site of integration, are the important factors that govern the expression of a transgene (Wall, page 61-62). The cis acting elements of one species may interact with different transactivating factors in other species. For example, the introduction of human growth hormone transgene in mice results in mammoth mouse phenotype, where as expression of the same transgene in pig results in premature death of transgenic pigs. (Pursel VG et al J. Reprod Fert. Sup 40: 235-245 1990, see page 235, para.1).

Furthermore, many biochemical pathways are plastic in nature, which reflects the ability of the embryo to use alternative gene when the preferred gene is modified. It is known in the art that the level and the specificity of a transgene as well as the phenotype of the transgenic animal are greatly dependent upon the specific expression vector used. The individual gene of interest, promoter, enhancer, coding or non-coding sequences present in the transgene construct and the site of integration, for example are the important factors that govern the expression of a transgene. (Kappel et al. Current Opinion in Biotechnology 3:558-553 1992; see page 550, col.1, para. 3-4, page 548, col.2 para.2).

Furthermore, the phenotype of targeted mutations by a homologous recombination have not always been as predicted because the homologous recombination is a rare event which requires numerous step that often fail. The embryonic stem (ES) cells are very sensitive to culture conditions and have natural tendency to differentiate, giving rise to unstable genome. The homologous recombination is a rare event in ES cells and the injection of ES in the blastocyte is

highly unpredictable (Viville, in Transgenic Animals, Houdebine (eds), Harwood academic publishers, France. pp307-321, 1997).

Thus, in view of lack of specific guidance in the specification and unpredictability in the transgenic art, the skilled artesian at the time of filing would be unable to use the invention as claimed, without an excessive and undue amount of experimentation. The quantity of experimentation required would include making of any and all non-human transgenic animals (insects, fish, reptiles, birds and mammals like whale, pigs, cow and elephant) encoding a transgene the contain a Fkh^{sf} coding sequence obtained from any and all organisms. The amount of experimentation required would further include phenotypic characterization of scurfy phenotypes across variety of species in animal kingdom and phenotypic evaluation of the Fkh^{sf} transgenic animals, wherein the Fkh^{sf} transgene has been obtained from any and all organisms.

Notice To Comply

Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Specifically the application fails to comply with CFR 1.821(d), which states:

(d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application (see MPEP 2422.03).

For compliance with sequence rules, it is necessary to include the sequence in the "Sequence Listing" and identify them with SEQ ID NO. In general, any sequence that is disclosed and/or claimed as a sequence, i.e., as a string of particular bases or amino acids, and that otherwise meets the criteria of 37 CFR 1.821(a), must be set forth in the "Sequence Listing." (see MPEP 2422.03).

The instant specification fails to comply with the requirements for patent applications containing nucleotide sequence and/or amino acid sequence disclosures. For example, the specification discloses nucleotide and/or amino acid sequences in Figures 1-4 and on pages 34-35 and 40. However, these sequences are not identified by a sequence identifier number (SEQ ID NO). In addition, the instant specification does not contain a paper copy and electronic diskette of sequence listing as required.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

For the response to this office action to be complete, Applicants are required to comply with the Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence.

A reply to a notice to comply with the sequence rules should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio
(**<http://www.uspto.gov/ebc/efs/downloads/documents.htm>**, EFS Submission User Manual - ePAVE)

2. Mailed to:
U.S. Patent and Trademark Office
Box Sequence, P.O. Box 2327
Arlington, VA 22202

3. Mailed by Federal Express, United Parcel Service or other delivery service to:

U. S. Patent and Trademark Office
2011 South Clark Place
Customer Window, Box Sequence
Crystal Plaza Two, Lobby, Room 1B03
Arlington, Virginia 22202

4. Hand Carried directly to the Customer Window at:
2011 South Clark Place
Crystal Plaza Two, Lobby, Room 1B03, Box Sequence,
Arlington, Virginia 22202

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Irem.Yucel can be reached on (703) 305-1998. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Zeta Adams, whose telephone number is (703) 305-3291.

S. Kaushal
Patent examiner

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER